THE RELATION OF ACHLORHYDRIA TO THE NUTRITIONAL ANÆMIA OF CHILDREN*

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ACHLORHYDRIA is commonly found in the hypochromic anæmia of adults and seems to be constantly associated with pernicious anæmia. It is of interest therefore to know what the relationship of achlorhydria is to the nutritional type of anæmia in childhood. Lightwood and Hawksley[1] have noted that 12 out of 13 successive cases of hypochromic anæmia in infancy had complete achlorhydria after alcohol test meals. In 4 of their cases the achlorhydria was present after the anæmia had been cured by iron. Similar results have been obtained by others and criticized by some.

It has been shown in adults (Mettier and Minot[2]) that replacement of acid alone will not produce a reticulocytosis, but that iron administered in an acid medium will promote a better response than iron administered in an alkaline medium. Barer and Fowler,[3] on the other hand, found by balance experiments that when iron was given in large quantities the amount retained was unaffected by gastric acidity. Their achlorhydric patients retained less iron from a normal dietary intake, but the addition of hydrochloric acid did not increase the retention of iron with either high or normal intake.

In the present report the data concerning the reticulocyte response when HCl was given by mouth to 3 patients with nutritional anæmia are presented.

Material.—Twelve children in all were observed. All save two were under five, although their ages varied between 10 months and 10 years. All had severe hypochromic anæmia.

An attempt was made to stabilize the reticulocyte count while under observation, and then to give HCl by mouth and watch the reticulocyte response. For various reasons, *e.g.*, premature removal from hospital and fear of intercurrent infection, only in three of these cases could the experiment be completed. In these it was possible to stabilize the reticulocyte count on the ward diet for an average period of 6 days. The patients were then given HCl for an average period of 11 days, and the reticulocytes counted regularly. Afterwards iron was given by mouth and the reticulocyte response again noted.

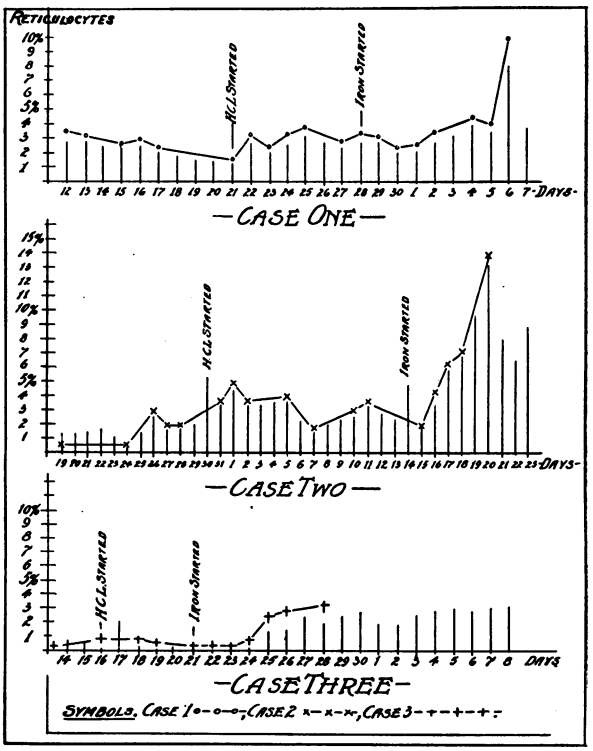
Procedure.—1. Gastric analyses.—The resting juice was removed and then either alcohol or histamine used to stimulate gastric secretion: 25 to 40 c.c. of a 7 per cent solution of alcohol or 5 to 7 m. of a 1:1,000 solution of histamine phosphate (hypodermically) were given. Afterwards specimens were collected every 15 minutes for 2 hours.

2. Treatment.—HCl (dil.) was given by mouth in doses from 15 to 30 minims every four hours, and later iron was given as ferrous sulphate 10 to 30 gr. daily according to age.

3. The reticulocytes were counted every day as far as possible, and at approximately the same hour.

4. The ordinary ward diet was given and no other medicine or treatment allowed.

Results.—The detailed reticulocyte response in the first three cases is shown in the Chart.



Chart

* A paper delivered before the Pædiatric Section of the Vancouver Medical Association.

TABLE

Case number	*Age*	*Sex*	*Red blood cells*	*Hæmoglobin*	*Color index*	*Gastric analyses*	*Remarks*
1	1 year 5 months	Male	3,600,000	43%	0.6	Complete achlorhydria.	Deficient diet. Very good reticulocyte response to iron; none to HCl.
2	4½ years	Male	3,000,000	30%	0.5	Complete achlorhydria (alcohol & histamine).	Deficient diet. Achlorhydria still present after cure with iron, 2 months later.
3	10 years	Male	4,300,000	55%	0.6	Complete achlorhydria (alcohol & histamine).	Evidence past mild nasopharyngeal infection. Achlorhydria persisted after cure with iron. Poor reticulocyte response to iron.
4	1 year 4 months	Female	3,540,000	35%	0.5	Complete achlorhydria (alcohol & histamine).	Good recticulocytosis after iron.
5	1 year 1 month	Female	3,900,000	45%	0.4	Hypochlorhydria; trace HCl in 1 specimen (histamine).	Deficient diet. Good recticulocyte response to iron.
6	2 years	Male	4,100,000	36%	0.4	Hypochlorhydria (histamine).	Very poor diet—prolonged milk feeding. Slight recticulocyte response to acid probably due to improved ward diet. Good response to iron.
7	5 years 5 months	Male	3,300,000	60%	0.9	Complete achlorhydria (histamine).	No recticulocyte response to 10 days acid. Evidence of past slight blood loss.
8	10 months	Female	2,100,000	22%	0.5	Complete achlorhydria (histamine).	Twin—Apparently most robust of the two until onset of anæmia.
9	10 months	Female	4,180,000	56%	0.7	Hypochlorhydria; trace free acid in 1 specimen (alcohol & histamine).	Twin—Had identical diet with sister. No additions to milk formula. Smallest and apparently least robust at birth—later was less anæmic than sister.
10	1 year 1 month	Female	4,000,000	40%	0.5	Hypochlorhydria (histamine).	Deficient diet.
11	10 months	Female	5,000,000	40%	0.4	Complete achlorhydria (alcohol).	Mixed feeding not started. No infection found.
12	1 year 5 months	Male	2,500,000	22%	0.44	Complete achlorhydria (alcohol).	Mixed feeding not started (mild urinary infection).

The clinical data in all the cases are shown in the Table. In no instance in any of the cases was there a significant rise in the number of reticulocytes while HCl was being given. The minor variations are probably accounted for by improved diet. In each case iron gave a definite reticulocyte response. The etiological factors present in the 12 cases were analyzed and the results are as follows: 9 out of the 12 patients had complete achlorhydria, and the rest had marked hypochlorhydria. Deficient diet was definitely present in 75 per cent of the cases, and it was due either to prolonged breast or milk feeding or to deprivation of greens or meat. Prematurity was present in three cases, and two of the patients were twins. Slight loss of blood was present in one case, and chronic infection was proved as a contributing factor in two instances. Toxic absorption was not found.

DISCUSSION

It is interesting to note that in the cases of the twins observed at this time the one which was heaviest and seemed the healthiest at birth became the more anæmic at ten months of age; the child which was apparently the weakest at birth became only very slightly anæmic. The former child had no free acid in the stomach, whereas the latter had normal acidity. They both had identical, but deficient, diets.

The present results suggest that acid-replacement therapy will not cause an immediate response of the marrow by the production of reticulocytes, and so confirms, by another method, the results of Barer and Fowler. The clinical evidence that achlorhydria is causally related to the anæmia is confirmed, but it still remains to be shown if *continuous treatment with acid* would improve the absorption of the

iron in the diet and so improve the anæmia. Evidently the hæmatinic effect of the acid is so slight as to be of no therapeutic value in this disease. Achlorhydria or *an associated deficiency in gastric secretion* may be the contributing factor in the causation of the nutritional anæmias, while diet deficiency is apparently the most common precipitating causative factor.

SUMMARY AND CONCLUSIONS

The negative results of the HCl treatment by mouth in cases of nutritional anæmia in children are reported and the relationship of achlorhydria to the causation of this type of anæmia is discussed.

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THE SIGNIFICANCE OF INDIGO, CYANOGEN AND THIOCYANATE IN TUMOUR CASES*

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IT was shown in a previous paper[1] that indigo occurs in the veins of rabbits. In the liver, in the vena cava and its branches, in the veins of the stomach, intestines and mesentery, the indigo was found to exist in a leuco form, and its detection depended upon oxidation to the blue form. As similar normal human tissues were not available, it is assumed that the indigo in these also exists in the leuco form. In view of the proposed explanation of the function of indigo that follows, it seems probable that it should exist in the leuco form in normal healthy internal organs, and that it would not be found in the blue form except in diseased conditions. Human tissues were available from malignant tumours of the liver and of abdominal lymph nodes. The indigo in the veins of these tumours was already in the blue form so that oxidation was an unnecessary part of the procedure for its detection.

In the paper referred to it was also shown that the indigosulphonates held calcium in a state of supersaturation in a phosphate-containing Ringer's solution. Consequently, it was suggested that the state of calcium supersaturation in most of the body fluids might also be due to the presence of indigo in the veins and capillaries. Such a function would seem secondary, and its primary function would seem more likely to depend upon its reversible oxidation-reduction properties. This view finds support in the fact that it has been found in the two forms, leuco in the veins of the liver and other abdominal organs of normal rabbits, blue in the veins of tumours of the liver and other human abdominal organs. It was probably found in the blue form because it had lost its ability to be reduced to the leuco form. The change from the more soluble leuco form to the less soluble blue form is probably part of a defensive mechanism in cases of accident to prevent loss of blood to the tissues in order to provide sufficient circulation in the brain to maintain consciousness. Such a defensive mechanism might operate in other emergencies like that of the rat described below. In all cases its efficiency would depend upon its complete reversibility. Should conditions be such that the less soluble blue form did not revert completely back to the more soluble white form, then it would gradually fill the vein and capillary walls and render them less permeable to the passage of oxygen and nutritive material. The resulting condition of the tissues would be quite comparable to that produced by ligating the inferior blood supply to the uterus of a rat.[2] The consequent malnutrition of the rat uterus would constitute a call for help that would probably be answered by the indigo mechanism in the veins and capillaries of the closely related mammary gland limiting diffusion of nutrition there in order to make more available

* From Mercy Hospital Institute of Radiation Therapy, Chicago.